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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/724,538

11/28/2000

Daniel D. Shoemaker

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7044

20583

7590

12/15/2006

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,538

Applicant(s)

SHOEMAKER ET AL.

Examiner

Frank W Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-34,36,45,46,86-90,157-181,183,212,213,263-267 and 280-296 is/are pending in the application.
- 4a) Of the above claim(s) 46,88,212,213,266 and 267 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-34,36,45,86,87,89,90,157-181,183,263-265 and 280-296 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 01 April 2003 is: a) ☒ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9/2006. 6) ☐ Other: _____

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DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission of RCE and the amendment filed on September 18, 2006 have been entered. The claims pending in this application are claims 1, 4-34, 36, 45, 46, 86-90, 157-181, 183, 212, 213, 263-267, and 280-296 wherein claims 46, 88, 212, 213, 266, and 267 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on September 18, 2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Enablement

Claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification

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in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods recited in claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 can be performed. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 can be performed.

Claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 are directed to a method for analyzing exon expression in a cell sample by measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes in the genome of an organism from which said cell sample is derived, wherein at least one gene in said plurality of different genes has an exon having a plurality of different variants, and measuring the expression level of each of said plurality of different variants of said exon in said at least one gene, each of said plurality of different variants

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being a different splice form of said exon generated using a different 3' or 5' splice junction of said exon. First, although expression levels of different individual exons or different individual multiexons can be measured either in mRNA level or protein level, since the claims are not limited to measure exon expression in mRNA level and the specification does not provide adequate guidance to measure expression levels of different individual exons or different individual multiexons in protein level, it is unclear how to measure expression levels of different individual exons or different individual multiexons in protein level. Second, since the claims can be read as a method for analyzing exon expression in *in vivo*, since the claims are not limited to a method in *in vitro* and does not indicate how to measure exon expression in *in vivo*, it is unclear how to measure exon expression in a cell sample in *in vivo*. Third, although applicant may argue that real-time RT-PCR can be used to measure expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes in the genome of an organism from which said cell sample is derived, since the claims do not require that the plurality of different genes are known genes and it is known that real-time RT-PCR different individual exons or different individual multiexons requires some primers with known sequences, it is unclear how to measure expression levels of a plurality of different individual exons or different individual multiexons in each of the plurality of different unknown genes in the genome of an organism with unknown sequences.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether

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the methods recited in claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265, 280-283, and 293-296 can be performed.

Conclusion

4. No claim is allowed.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746.

The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

December 11, 2006



FRANK LU
PRIMARY EXAMINER